November 7, 2004

C. Andrew Waters
Waters & Kraus, LLP
3219 McKinney Avenue
Dallas, TX 75204

Dear Mr. Waters,

Enclosed, please find a copy of my report containing my opinions regarding the capability of the mercury in Thimerosal to cause neurological damage in infants who have received vaccines. This information is supplemented by my published papers, the presentations that I have given on this subject, and any subsequent depositions given by me on this subject. As new information is developed, I will endeavor to supplement this report.

Sincerely,

M. Geier

Dr. Mark R. Geier

Encls

I have an M.D., with a Ph D. in genetics. I am president of the Genetic Centers of America, and have been in clinical practice for more than 20 years. I have previously been a researcher at the National Institutes of Health (NIH) for 10 years. I was also a professor at the Johns Hopkins University and at the Uniformed Services University of the Health Sciences.

I have worked in the field of vaccinology (i.e. the study of vaccines) for over thirty years. My first involvement in this field was during my ten years of work at the NIH. In 1971, the research group that I worked with received national and international acclaim including front page news coverage for our publication, which was the first demonstration that bacterial genes could function in human cells in vitro to correct a human inborn error of metabolism.[1] Since this was the first successful genetic engineering experiment, each of the members of the research group, including myself, received personal congratulations on their ground breaking work from President Nixon. In order to try to make progress toward using the viral vector developed by the researchers, the bacteriophage lambda, to carry genes into humans, my research associates and I began to study what happened when this virus was injected into germ-free mice. The results of the research showed that the spleen was not a residual organ, but that the spleen played an important role in mounting an effective antibody response.[2] This ground breaking work, was of considerable importance to vaccines because the spleen plays an important role in successful vaccine response. The work lead to the understanding that surgeons should spare the spleen whenever possible, and that among those patients with their spleens removed would not respond well to vaccines and other antigens. This work marked the beginning of my lifelong involvement in the vaccine field. My research group published a number of additional papers on the function of the spleen.[3] My research group also published a study on ways to try to modify the way in which foreign antigen was handled by studying the effect of a second interfering antigen on the intrinsic immune system.[4]

In 1973, while working on a bacteriophage human tissue culture model system, my research group also discovered that fetal calf serum contained large amounts of various types of bacteriophages.[5] Since this was the same fetal calf serum that was used in the production of various vaccines, my research group soon thereafter discovered that human vaccines were also contaminated with large numbers and types of bacterial viruses. By law all viral vaccines had to contain only one viral strain. This law was originally introduced to end the contamination of polio vaccine with SV40 virus. Therefore, a FDA

[1] Merril CR, Geier MR, Petricciani J. Bacterial virus gene expression in human cells. Nature 1971; 233:398-400.
[2] Geier MR, Trigg ME, Merril CR. The fate of bacteriophage lambda in non_immune germfree mice. Nature 1973;246:221.
[3] Trigg ME, Geier MR, Merril CR. Trapping of antigen in spleen. N Eng J Med 1975;292:214.
Trigg ME, Geier MR, Merril CR. Comparative distribution and splenic accumulation of bacteriophage lambda in conventional mice. International Research Communications System 1975;5:261.
[4] Geier MR, Kamerow HM, Merril CR. The effect of large and small rubber particles on the distribution of bacteriophage in conventional mice." International Research Communications System 1975; 5:493.
[5] Merril CR, Friedman TB, Attallah A, Krell K, Geier MR, Yarkin R. Isolation of bacteriophages from commercial sera. In Vitro 1972;8:91-3.

conference was called to address this problem and at this conference, I was invited to present the results of his research." One of the major components of my dissertation involved my work on vaccines.[7] Although I have never made a vaccine, I am quite familiar with the processes used in manufacturing many vaccines because during my ten year tenure at the NIH, I operated the NIH pilot plant, which is the same plant later used at the NIH to make pertussis vaccines. I have also inspected vaccine production plants in both the US and Canada.

In 1978, I began to study endotoxin levels in vaccines.[8] This study was the beginning of my more than 20 year involvement in helping to get the US whole-cell Diphtheria-Tetanus-Pertussis (DTP) vaccine replaced by the much safer acellular Diphtheria-Tetanus-acellular-Pertussis (DTaP) vaccine, which was finally completed in the US by 2001.

During my more than thirty years as a vaccinologist, I have published more than 50 peer-reviewed scientific/medical papers on vaccine safety, efficacy, contamination, and policy. These papers have been published in a wide variety of peer-reviewed scientific/medical journals, including: general medical journals, pediatric journals, state medical journals, immunological journals, pharmacological journals, gastroenterology journals, rheumatology journals, pediatric neurology journals, history of medicine journals, etc. I have published on vaccine related issues in such journals as *Nature*, the *New England Journal of Medicine*, and *Experimental Biology & Medicine*. I have been invited to write peer-reviewed scientific/medical papers on vaccines and methods of monitoring vaccine safety for the highly prestigious expert opinion journal series.[9] I have received critical acclaim from his colleagues for his research on vaccines by winning the "Stanley W. Jackson Prize," which is given to authors having the best paper in the preceding three years in the *Journal of the History of Medicine and Allied Sciences* published by Duke University.[10] I have also served as a peer-reviewer on vaccine/drug issues for prestigious scientific/medical journals, including: *Vaccine*, *Expert Review of Vaccines*, *Annals of Internal Medicine*, *Expert Opinion on Emerging Drugs*, *Clinical and Experimental Rheumatology*, and *Environmental Health Perspectives*.

I have been invited to make presentations to the Institute of Medicine (IOM) of United States' National Academy of Sciences on six occasions, twice during 2004. I have addressed the Food and Drug Administration (FDA) Advisory Committee regarding

---

[6] Geier MR, Trigg ME, Merril CR. A model system for the evaluation of the fate of phage in contaminated vaccines: Physiologic disposition of bacteriophage in mice. Proceedings of the Workshop of Problems of Phage Contamination. FDA. 1973.
[7] Geier MR. The Effect of Prokaryotic Genes in Eukaryotes. Ph.D. Dissertation submitted to The George Washington University 1973
[8] Geier MR, Stanbro H, Merril CR. Endotoxins in commercial vaccine. Applied and Environmental Microbiology 1978; 36:445-9.
[9] Geier MR, Geier DA, Zahalsky AC. A review of hepatitis B vaccination. Expert Opin Drug Saf 2003;2:113-22.
Geier DA, Geier MR. A review of the Vaccine Adverse Event Reporting System database. Expert Opin Pharmacother 2004;5:691-8.
[10] Geier DA, Geier MR. The true story of pertussis vaccination: A sordid legacy? J Hist Med Allied Sci 2002;57:249-84

vaccine safety. In 2002, I was invited to testify before the Government Reform Committee of the United States House of Representatives regarding vaccine safety issues. My co-researchers and I, with the help of Congressman Burton and Congressman Dr. Dave Weldon, were the first and only independent researchers allowed to study the previously proprietary Vaccine Safety Datalink (VSD) database of the Centers for Disease Control and Prevention (CDC). In addition, I have been invited to speak on vaccine issues to numerous US Senators and Representatives, and their senior health staffs, as well as to numerous state Attorney Generals. I have been invited to give numerous talks on vaccine issues by various scientific, legal, health department, and parent groups in the US and around the world. I have also attended many government sponsored conferences on vaccines, and I have attended and spoken at many courses on vaccines, including the NIH graduate school course on Vaccines in 2002, and the NIH graduate school course on emerging infectious diseases in 2003.

My work on vaccines has been covered by state and national news media, and has been seen on TV. It has been the subject of numerous magazine articles and documentaries. I have appeared as an expert on numerous local and national radio and TV shows.

I have been accepted as an expert witness in numerous Federal courts and state courts, as well as in Canadian and English courts. I have also been accepted as an expert witness in approximately 100 cases before the National Vaccine Injury Compensation Program (NVICP) of the US Court of Federal Claims.[11] I have recently passed a Daubert challenge on my opinions on vaccine matters in Federal Court in Ohio.[12] My vaccine opinions have recently survived a Daubert and Fry challenge in Pennsylvania state court.[13]

My rate of compensation for offering opinions in this case is $250.00 per hour. I have also attached a copy of my CV and a list of the cases I have participated in (Attachments A and B).

Background: An Assessment of Neurodevelopmental Disorders in the United States

In considering neurodevelopmental disorders, one that has received considerable attention in recent years is autism. Autism is a lifelong neurodevelopmental disorder that primarily strikes males. Communication and social interactions are severely impaired for persons with autism. Unable to learn from the natural environment as most children do, the child with autism generally shows little interest in the world or people around him. Although some children with autism develop normal and even advanced skills, most exhibit a wide range of behavioral problems. Autism, in reality, is a lifelong

[11] Estep v. HHS, No. 90-1062V, June 25, 1993; McClendon v. HHS, No. 90-579V, September 25, 1991.
[12] Jeffries v. Centre Life Insurance Company, et al., Civil Action No. C-1-02-351, Cincinnati, Ohio, United States District Court, Southern District of Ohio, Western Division.
[13] James Landi & Roxanna Landi v. Wyeth-Ayerst Laboratories et al. Philadelphia County Court of Common Pleas December Ter. 2001, No.: 4443.

developmental disability that profoundly affects the way a person comprehends, communicates and relates to others.[14]

The best statistics indicate that prevalence of autism has increased from 7.5 per 10,000 children (1 **in 1,333 children**) among children born in the mid-1980s to 31.2 per 10,000 children (**1 in 323 children**) among children born in the late-1990s, an approximate 4-fold increase in childhood autism in about one decade. Between 1987 and December 2002, it is estimated that population of persons with autism increased by **634 percent**. Autism, once a rare disorder, is now more prevalent than childhood cancer, diabetes and Down Syndrome. It has been determined that explanations such as immigration, or shifts in diagnostic criteria cannot explain the observed increase, and the phenomena is driven by factors beyond improved identification and diagnosis.[15]

Similarly, studies conducted by Yeargin-Allsopp et al. and Bertrand et al., both from the CDC, have reported that they observed a higher prevalence of autism than was observed in previous studies, and that the higher prevalence of autism they observed was more consistent with recent studies.[16] Bertrand et al. reported that the overall prevalence of all autism spectrum disorders combined was 6.7 cases per 1,000 children (**1 in 149 children**), and the overall prevalence for children whose condition met the full diagnostic criteria for autistic disorder was 4.0 cases per 1,000 children (**1 in 250 children**). Yeargin-Allsopp et al. reported that the overall prevalence for autism was 3.4 cases per 1,000 (**1 in 294 children**), with a **male-female ratio 4:1**.

In addition, both studies observed that the younger children examined had higher prevalence rates of autism in comparison to the older children examined. Yeargin-Allsopp et al. observed that the prevalence of autism was between approximately 4 to 5 cases per 1,000 children among children aged 5 to 8 years-old, where as the prevalence of autism was approximately between approximately 2 to 2.5 cases per 1,000 children among children aged 9 to 10 years-old. Bertrand et al. observed that the prevalence of autism was 5.5 cases per 1,000 children (**1 in 182 children**) among children age 3 to 5 years-old, whereas the prevalence of autism was 3.1 cases per 1,000 children among children age 6 to 10 years-old. Bertrand et al. also observed that the prevalence of autism spectrum disorders combined was 7.8 cases per 1,000 children (**1 in 128 children**) among children age 3 to 5 years-old where as the prevalence of autism spectrum disorders combined was 6.1 cases per 1,000 children among children aged 6 to 10 years-old. The observations by Yeargin-Allsopp et al. and Bertrand et al. add additional evidence to support that the rate of autism in the United States for the following reasons, including: (1) issues relating to different ascertainment of cases that may account for differences in the observed prevalence were minimized [i.e. the case ascertainment was

[14] California Department of Developmental Services. Autistic Spectrum Disorders – Changes in the California Caseload - An Update: 1999 Through 2002. Sacramento, CA: State of California, April 2003.
[15] California Department of Developmental Services. Autistic Spectrum Disorders – Changes in the California Caseload – An Update: 1999 Through 2002. Sacramento, CA: State of California, April 2003.
[16] Yeargin-Allsopp M, Rice C, Karapurkar T, Doernberg N, Boyle C, Murphy C. Prevalence of autism in a US metropolitan area. JAMA 2003;289:49-55.
Bertrand J, Mars A, Boyle C, Bove F, Yeargin-Allsopp M, Decouflé P. Prevalence of autism in a United States population: the Brick Township, New Jersey, investigation. Pediatrics 2001;108:1155-61.

consistent within each study]; (2) one would expect, since a number of years may be required for a child to receive a diagnosis of autism, that inherently more older children should be diagnosed with autism because they have had a greater follow-up period than younger children, but despite this fact, it was observed that the younger children tended to have a higher prevalence of autism than the older children examined.

There are other researchers that have shown an increase in autism in the United States.[17]

The most recent estimates, as per the Autism ALARM that was issued in January 2004 by the American Academy of Pediatrics (AAP) and the CDC, state that **1 in 166 children** in the United States suffers from an autism spectrum disorder, and far worse that **1 in 6 children** suffers from a developmental and/or behavior disorder.

What is Thimerosal?

Thimerosal (Merthiolate, Thiomersal) is preservative that has been added to some vaccines since the 1930s. It is approximately **50% ethylmercury** (organic mercury) by weight. Thimerosal is broken down into ethylmercury residues, and the ethylmercury residues are eventually broken down to ionic inorganic mercury.[18] Thimerosal has been recognized by the state of California as a **developmental toxin**, meaning that it can cause birth defects, low birth weight, biological dysfunctions, or psychological or behavior deficits that become manifest as the child grows, and maternal exposure during pregnancy can disrupt the development or even cause the death of the fetus.[19]

Accidental Human & Animal Population Exposures to Ethylmercury

From the 1950s-1960s, a series of population outbreaks of ethylmercury poisonings occurred in Iraq following ingestion of Granosan M that was used against plant root disease of wheat. Since 1955, the Iraqi Ministry of Agriculture supplied farmers with seeds dusted with the fungicide. Farmers have frequently been warned against using the seed for food, and most of them are aware of the highly lethal effect of dusted seeds. Out of ignorance or neglect however, some unfortunate farmers were the victims of the fungicide after eating the dusted seeds. As a result, these farmers developed a number of mercury related serious conditions.[20] Specifically, it was reported [emphasis added]:

---

[17] Blaxill MF, Baskin DS, Spitzer WO. Commentary: Blaxill, Baskin, and Spitzer on Croen et al. (2002). the changing prevalence of autism in California. J Autism Dev Disord 2003;3:223-6.
Gerlai J, Gerlai R. Autism: a target of pharmacotherapies? Drug Discov Today 2004;9:566-74.
Gerlai J, Gerlai R. Autism: a large unmet medical need and a complex research problem. Physiol Behav 2003;79:461-70.
Yazbak FE. Autism in the United States: a preservative. J Am Phys 2003;8:103-7.
Gurney JG, Fritz MS, Ness KK, Sievers P, Newschaffer CJ, Shapiro EC. Analysis of prevalence trends of autism spectrum disorder in Minnesota. Arch Pediatr Adolesc Med 2003;157:622-7.
[18] Tan M, Parkin JE. Route of decomposition of thiomersal (thimerosal). Int J Pharm 2000;208:23-34.
[19] California Environmental Protection Agency - Office of Environmental Health Hazard Assessment. Response to the petition of Bayer Corporation for clarification of the Proposition 65 listing of "Mercury and Mercury Compounds" as chemicals known to cause reproductive toxicity. February 2004.
[20] Jalili MA, Abbasi AH. Poisoning by ethyl mercury toluene sulphonanilide. Br J Ind Med 1961;18:303-8.
Samuji S. Mercurial poisoning with e fungicide Granosan M. J Fac Med Baghdad 1962;4:83-103.

Poisoning by a fungicide used for seed-borne diseases of cereals, ethyl mercury p-toluene sulphonanilide (Granosan M, Dupont) is described. It affected a large number of farmers and their families who used the dressed seed in the preparation of home-made bread. Many systems were involved, including the kidneys, the gastrointestinal tract, the skin, the heart, and the muscles, but ***involvement of the nervous system was the most constant with disturbance of speech, cerebellar ataxia, and spasticity. Mental abnormalities were occasionally observed.****..In 1956 many cases of mercury poisoning were observed in the North of Iraq, and more than 100 cases were admitted to Mosul Hospital with 14 deaths. In 1960, many farmers from the central part of Iraq were affected and 221 patients were admitted to one hospital in Baghdad. Other patients went to other hospitals.*[21]

In 1972, Spann et al. from the Bureau of Sport Fisheries and Wildlife, Patuxent Wildlife Research Center reported in *Science* regarding the lethal and reproductive effects of ethylmercury on pheasants. The stated:

Ethyl mercury p-toluene sulfonanilide (active ingredient of Ceresan M) at a dietary concentration of 30 parts per million (12.5 parts of mercury per million) was lethal to adult ring-necked pheasants. Egg production and survival of third-week embryos were sharply reduced when breeders were maintained on feed containing 10 parts of this compound per million (4.2 parts of mercury per million)...Since similar residues of mercury have been found in eggs of wild pheasants and several species of aquatic birds, we conclude that mercury pollution may be sufficiently high in some areas to affect avian reproduction.[22]

In 1977, Mukhtarova reported on the late after-effects of the nervous system following chronic low-dose exposure to ethylmercuric chloride. The researcher reported:

A total of 25 persons exposed to multiple effects of low ethyl-mercuric-chloride concentrations were subjected to a clinical examination in dynamics 1 ½ and 3 years after exposure to the compound. In investigations clinico-physiological (EEG, Asschner-Dagnini reflexes, etc) and biochemical (catecholamines, sugar, mercury, DDT, DDE in the urine, etc) methods were employed. The pathology of the nervous system presented certain peculiarities by comparison with early period. In evidence were changes in the simpatico-adrenal system function, vascular lesions of the brain after the type of transient derangements of the cerebral circulation in the vertebro-basilar basin and angiospasms, diffuse

---

Dahlum SS, Orfaly H. Mercury poisoning and electrocardiographic changes. J Fac Med Baghdad 1962;4:101-17.
Al-Kassab S, Saigh N. Mercury and calcium excretion in chronic poisoning with organic mercury compounds. J Fac Med Baghdad 1962;4:118-123.
[21] Jalili MA, Abbasi AH. Poisoning by ethyl mercury toluene sulphonanilide. Br J Ind Med 1961;18:303-8.
[22] Spann JW, Heath RG, Kreitzer JF, Locke LN. Ethyl mercury p-toluene sulfonanilide: lethal and reproductive effects on pheasants. Science 1972;175:328-31.

changes in the nervous system with predominant involvement of the hypothalamic cerebral structures and in some cases psychic disturbances were on record.[23]

Cinca et al. reported in 1979 on accidental ethylmercury poisoning with nervous system, skeletal muscle, and myocardium injury. The authors stated:

Four cases are presented of patient who ate the meat of a hog inadvertently fed seed treated with fungicides containing ethylmercury chloride. The clinical, electrophysiological, and toxicological, and in two of the patients the pathological data, showed that this organic mercury compound has very high toxicity not only for the brain, but also for the spinal motoneurones, peripheral nerves, skeletal muscles, and myocardium.[24]

Zhang in 1984 reported on clinical observations in patients with ethylmercury chloride poisoning. He stated:

Forty-one patients in the Peoples Republic of China were poisoned by ethyl mercury chloride, caused by the ingestion of rice that had been treated with the chemical. A dose-response relationship was found. Five months after the onset of the intoxication, the patients were still in poor condition. They were treated with two chelating agents, sodium dimercaptopropane sulfonate (DMPS) and sodium dimercaptosuccinate (DMS), whose effects were compared. Both agents were effective but DMPS was superior. Although urinary excretion is not the best estimate of body burden in alkyl mercury intoxication, during chelation therapy urinary mercury was an effective indicator for diagnosis and assessment of the degree of intoxication. Chelation therapy was diagnosis and assessment of the degree of intoxication. Chelation therapy was useful as long as the urinary mercury level was elevated.[25]

A Comparison of Ethylmercury & Methlmercury

In considering organic mercury compounds, one that has received considerable attention in recent years is methylmercury. The US FDA has recommend that pregnant women, women of childbearing age, and young children avoid eating shark, swordfish, mackerel, and tilefish because these fish often harbor high levels of methylmercury, a potent human neurotoxin. Methylmercury readily crosses the placenta and has the potential to significantly damage the fetal nervous system.[26] The National Research Council of the United States' National Academy of Sciences has concluded that the evidence is

[23] Mukhtarova ND. Late sequelae of nervous system pathology caused by the action of low concentrations of ethyl mercury chloride. Gig Tr Prof Zabol 1977 Mar(3):4-7.
[24] Cinca I, Dumitrescu I, Onaca P, Serbanescu A, Nestorescu B. Accidental ethyl mercury poisoning with nervous system, skeletal muscle, and myocardium injury. J Neurol Neurosurg Psychiatry 1980;43(2):143-9.
[25] Zhang J. Clinical observations in ethyl mercury chloride poisoning. Am J Ind Med 1984;5:251-8.
[26] Evans EC. The FDA recommendations on fish intake during pregnancy. J Obstet Gynecol Neonatal Nurs 2002;31:715-20.

compatible with chronic low-dose methylmercury exposure causing childhood developmental disorders.[27]

The peer-reviewed scientific/medical literature supports that ethylmercury and methylmercury compounds are at the very least similarly toxic.

Tan and Parkin have published regarding the chemical similarities of ethyl- and methylmercury:

> *The reactivity and complexation characteristics of the EtHg [ethylmercury] ion has never been investigated but the homologous methylmercury ion has received considerable attention due to its environmental toxicity. It would be expected that the EtHg ion would display similar complexation and chemical characteristics.*[28]

Suzuki et al. have published regarding the similarities of ethyl- and methylmercury mercury [emphasis added]:

> ***The toxic nature of ethylmercury has been considered to be fairly similar to that of methylmercury salts. In the recommendation of an international committee on Maximum Allowable Concentration for mercury and its compounds, ethylmercury was grouped with methylmercury salts. Reports on human intoxication with ethylmercury salts have usually reported symptoms similar to those of emthylmercury poisoning,*** *which is accentuated by the typical neurological symptoms, although there have been a few reports that noted slightly different symptoms from the typical features of methylmercury poisoning.* ***In acute experiments on aminals, ethylmercury has an LD_{50} similar to that of methylmercury salts and a high neurotoxicity similar to that of methylmercury and n-propylmercury salts.*** *In relation to neurotoxicity expressed as mercury content in the brain when neurological symptoms appear, the toxic dose of ethylmercury was suggested to be higher than that of methylmercury salts. In comperative studies on bodily distribution of mercury after administration of alkylmercury salts in mice or rats, ethylmercury showed a lightly different pattern from methylmercury and n-propylmercury salts...* ***The biological half-life times of mercury in the whole brain or each compartment of mice after methylmercury and phenylmercury injections are reported to be six to seven days and 14 to 20 days, respectively. The calculated total mercury in the brain after intravenous injection of ethylmercury chloride was 21.4 days in the present experiment...***[29]

Zhang as reported regarding the toxicological similarities of ethyl- and methylmercury [emphasis added]:

---

[27] National Research Council (US). Toxicological Effects of Methylmercury. Washington, DC: National Academy Press, 2000.
[28] Tan M, Parkin JE. Route of decomposition of thiomersal (thimerosal). Int J Pharm 2000;208:23-34.
[29] Miller MW, Clarkson TW (Eds). Mercury, Mercurials and Mercaptans. Suzuki T, Takemoto T, Kashiwazaki H, Miyama T. Chapter 12. Metabolic fate of ethylmercury salts in man and animal. Springfield, IL: Charles C. Thomas Publisher, 1973, pgs. 209-32.

> ***Ethyl mercury compounds have toxicological properties similar to those of methyl mercury compounds.*** *There is evidence that both methyl and ethyl mercury can persist in the body for a long time.*[30]

Ball et al., from the Office of Vaccine Research and Review within the FDA, have reported regarding ethyl- and methylmercury [emphasis added]:

> *Because high-dose exposure to ethylmercury from thimerosal results in toxicity comparable to that observed after high-dose exposure to methylmercury, and because of the chemical similarity of the 2 compounds,* ***it appears reasonable to consider toxicity of low doses of methylmercury and ethylmercury to be similar.***[31]

Yonaha et al. have evaluated ethyl- and methylmercury, and reported [emphasis added]:

> *The clinical signs and pathological findings caused by methylmercury compounds in animal experiments were known to be similar to Minamata disease manifested in human.* ***At the same time, the symptoms in cats, calves, and mice poisoned by ethylmercury compounds were similar to those in methylmercury compounds.*** *Further, as reported by Sebe et al., alkylmercury compounds having short carbon chains (C_1-C_3) bring about the specific neurotoxicity and the signs of poisoning in rats, which are consisted of weight loss, ataxia, and closing of the hindlegs. Saito et al. reported the dolphin kick convulsion as a criterion for experimental Minamata disease in mice.*[32]

Chao et al. conducted *in vitro* studies using HeLa cells that showed ethylmercury was at least similarly toxic or more toxic than other mercurials such as methylmercury, dimethylmercury, phenylmercuric acetate, *p*-hydroxymercuribenzoate, and *p*-hydroxymercuribenzenesulfonate, among others, depending on the exact outcome measure examined.[33]

Ucha-Ishibashi et al., from the University of Tokushima, have conducted an *in vitro* study that examined the toxic effects of thimerosal in comparison to methylmercury on rat cerebellar neurons.[34] The researchers reported [emphasis added]:

---

[30] Zhang J. Clinical observations in ethyl mercury chloride poisoning. Am J Ind Med 1984;5:251-8.
[31] Ball LK, Ball R, Pratt RD. An assessment of thimerosal use in childhood vaccines. Pediatrics 2001;107:1147-54.
[32] Yonaha M, Ishikura S, Uchiyama M. Toxicity of organic compounds. III. Uptake and retention of mercury in several organs of mice by long term exposure of alkoxyethylmercury compounds. Chem Pharm Bull 1975;23:1718-25.
[33] Chao ESE, Gierthy JF, Frenkel GD. A comparative study of the effects of mercury compounds on cell viability and nucleic acid synthesis in HeLa cells. Biochem Pharmacol 1984;33:1941-5.
[34] Ucha-Ishibashi T, Oyama Y, Nakao H, Umebayashi C, Nishizaki Y, Tatsuishi T, Iwase K, Murao K, Seo H. Effect of thimerosal, a preservative in vaccines, on intracellular Ca^{2+} concentration of rat cerebellar neurons. Toxicology 2004;195:77-84.

The effect of thimerosal, an organomercurial preservative in vaccines, on cerebellar neurons dissociated from 2-week-old rats was compared with those of methylmercury using a flow cytometer with appropriate fluorescent dyes. Thimerosal and methylmercury at concentrations ranging from 0.3 to 10 microM increased the intracellular concentration of Ca2+ ([Ca2+]i) in a concentration-dependent manner. The potency of 10 microM thimerosal to increase the [Ca2+]i was less than that of 10 microM methylmercury. Their effects on the [Ca2+]i were greatly attenuated, but not completely suppressed, under external Ca(2+)-free condition, suggesting a possibility that both agents increase membrane Ca2+ permeability and release Ca2+ from intracellular calcium stores. The effect of 10 microM thimerosal was not affected by simultaneous application of 30 microM L-cysteine whereas that of 10 microM methylmercury was significantly suppressed. The potency of thimerosal was similar to that of methylmercury in the presence of L-cysteine. Both agents at 1 microM or more similarly decreased the cellular content of glutathione in a concentration-dependent manner, suggesting an increase in oxidative stress. ***Results indicate that thimerosal exerts some cytotoxic actions on cerebellar granule neurons dissociated from 2-week-old rats and its potency is almost similar to that of methylmercury.***

Miller et al. have evaluated the distribution of mercury in chicks following injection of 3.0 mg of mercury as ethylmercuric chloride or methylmercuric chloride. The researchers found that mercury similarly distributed in chicks injected with ethylmeruric chrloride or methylmercuric chloride.[35]

Brooks et al. have conducted a pharmacokinetic study to evaluate the concentration of mercury present in blood of rats dosed orally with 8 mg / Kg mercury as methylmercury chloride or ethylmercury chrloride. The researchers demonstrated that mercury distributed similarly in the blood following oral dosing of rats with methylmercury or ethylmercury.[36]

Magos et al. have evaluated the toxicities of ethylmercury and methylmercury in rats.[37] The researchers reported [emphasis added]:

Neurotoxicity and renotoxicity were compared in rats given by gastric gavage five daily doses of 8.0 mg Hg/kg methyl- or ethylmercuric chloride or 9.6 mg Hg/kg ethylmercuric chloride. Three or 10 days after the last treatment day rats treated with either 8.0 or 9.6 mg Hg/kg ethylmercury had higher total or organic mercury concentrations in blood and lower concentrations in kidneys and brain than methylmercury-treated rats. In each of these tissues the inorganic mercury concentration was higher after ethyl- than after methylmercury. ***Weight loss***

[35] Miller VL, Klavano PA, Jerstad AC, Csonka E. Absorption, distribution, and excretion of ethylmercuric chloride. Toxicol Appl Pharmacol 1961;3:459–468.
[36] Brooks AG, Bailey E, Snowden RT. Determination of methyl- and ethylmercury in rat blood and tissue samples by capillary gas chromatography with electron-capture detection. J Chromatogr 1986;374:289-96.
[37] Magos L, Brown AW, Sparrow S, Bailey E, Snowden RT, Skipp WR. The comparative toxicology of ethyl- and methylmercury. Arch Toxicol 1985;57:260-7.

> *relative to the expected body weight and renal damage was higher in* ***ethylmercury-treated rats than in rats given equimolar doses of methylmercury.*** *These effects became more severe when the dose of ethylmercury was increased by 20%...* ***There was little difference in the neurotoxicities of methylmercury and ethylmercury when effects on the dorsal root ganglia or coordination disorders*** *were compared. Based on both criteria, an equimolar dose of ethylmercury was less neurotoxic than methylmercury, but a 20% increase in the dose of ethylmercury was enough to raise the sum of coordination disorder scores slightly and ganglion damage significantly above those in methylmercury-treated rats.*

In experiments supported by the *Canadian Medical Research Council* that evaluated chronic low-dose *in vivo* exposure to methylmercury and ethylmercury containing compounds.[38] The researchers reported [emphasis added]:

> *The resulting toxicosis was primarily related to the nervous system, in which neuronal necrosis followed by secondary gliosis, capillary endothelial proliferation, and additional neuronal necrosis due to developing degenerative arteriopathy in the blood vessels supplying injured gray matter were seen. In other systems, degeneration of hepatocytes and renal tubular cells were commonly occurring lesions in pigs given both MMD [methylmercury-containing compound] and EMC [ethylmercury-containing compound]...The results proved that the alkylmercurial compounds MMD and EMC, if fed at low concentrations for long periods, were highly poisonous to swine...* ***Comparatively, EMC proved much more toxic than MMD.***

A Brief History of Thimerosal Problems

Eli Lilly and Company of Indianapolis licensed Thimerosal in 1930. It was marketed under the brand name 'Merthiolate.' It was used extensively both in topical ointments to prevent infections and as a preservative in a variety of medicines.[39]

Smithburn et al. conducted the only human trial with Thimerosal (Merthiolate) during an epidemic of 144 cases of meningococcic meningitis that were admitted to the Indianapolis City Hospital between November 11, 1929, and April 1, 1930, primarily among what the authors stated were employees or relatives of employees in two departments of a large industrial concern (i.e. from the Lilly Laboratories for Clinical Research, Indianapolis City Hospital).[40] The only statements by the authors regarding Thimerosal (Merthiolate) were as follows:

---

[38] Tryphonas L, Nielsen NO. Pathology of chronic alkylmercury poisoning in swine. Am J Vet Res 1973;34:379-392.
[39] Subcommittee on Human Rights and Wellness, Government Reform Committee. Mercury in Medicine Report. Washington, DC: Congressional Record, May 21, 2003:E1011-30.
[40] Smithburn KC, Kempf GF, Serfas, Gilman LH. Meningococcic meningitis – a clinical study of one hundred and forty-four epidemic cases. JAMA 1930;95:776-80.

The treatment has remained essentially the same throughout the epidemic. The routine adopted included on admission, a skin sensitization test, rhachicentesis and intrathecal serum, intramuscular serum and (especially during the second month of the epidemic) serum intravenously. Intravenous administration of an antiseptic solution was tried and found wanting despite the in vitro activity of the agent...

The procedure finally adopted was: ephedrine sulphate, 3 percent, in each nostril followed by sodium-ethylmercuri-thiosalicylate (Merthiolate) 1:4,000 twice daily. Following the institution of this therapy no nasopharyngeal cultures were positive. Further than the foregoing, the treatment was symptomatic.

In 1931, the Smithburn et al. study, was followed by a study by Powell and Jamieson from the Research Laboratories, Eli Lilly Company, on Merthiolate (Thimerosal) as a germicide.[41] The researchers reported on the toxicity of Merthiolate (Thimerosal) in man:

Merthiolate has been injected intravenously into 22 persons in doses up to 30 cubic centimeters of 1 percent solution. As many as five intravenous doses, or a total of 180 cubic centimeters of 1 percent Merthiolate, have been given to one individual (see table 7). These large doses did not produce any anaphylactoid or shock symptoms. Neither did these quantities in the repeated doses bring about any demonstrable later toxic effects. The toleration of such intravenous doses indicates a very low order of toxicity of Merthiolate for man. This information has been supplied through the kindess of Dr. K.C. Smithburn of Indianapolis who has had occasion to use Merthiolate in a clinical way. Dr. Smithburn stated that in these cases "beneficial effect of the drug was not definitely proven. It did not appear however to have any deleterious action when used in rather large doses intravenously when all the drug entered the vein."

It should be noted that the Powell and Jamieson article did not even quote the study by Smithburn et al. (i.e. there is no reference at all in the Powell and Jamieson article for their statements about Thimerosal (Merthiolate). In considering the information provided by Powell and Jamieson in Table 7 on the 22 patients that received Thimerosal (Merthiolate), it is important to keep in mind the following factors that were not even mentioned/considered: (1) The 22 patients that were administered Thimerosal (Merthiolate) were all sick with meningitis at the time, so that any adverse effects induced by the administration of Thimerosal (Merthiolate), it was not clear whether they were the result of the ongoing infection of the treatment; (2) Approximately 1/3rd of the 22 patients reported on were only followed-up for one day following treatment, and among all 22 patients examined the maximum numbers of days of follow-up was only 62 days, so it would have been difficult to discern the acute adverse effects of Thimerosal (Merthiolate) [i.e. within 30 days], let alone chronic conditions that developed over several months.

[41] Powell HM, Jamieson WA. Merthiolate as a germicide. Am J Hyg. 1931;13:296-310.

By 1935, the Pittman-Moore Company, despite the earlier conclusion reached by Powell and Jamieson of the relative non-toxicity of Thimerosal (Merthiolate), had already demonstrated that Merthiolate (Thimerosal) was not appropriate for use in dogs [emphasis added]:

> *We have obtained marked local reaction in about 50% of the dogs injected with serum containing dilutions of Merthiolate, varying in 1 in 40,000 to 1 in 5,000, and we have demonstrated conclusively that there is no connection between the lot of serum and the reaction.* ***In other words, Merthiolate is unsatisfactory as a preservative for serum intended for use on dogs.*** *Occasional dogs do not show the local reaction, but in some instances, the reaction is extremely severe. I might say that we have tested Merthiolate on humans and find that it gives a more marked local reaction than does phenol or tricresol.*[42]

Warkany and Huber reported in 1953:

> *In several children of our series and in some recently reported, various immunization procedures preceded the onset of acrodynia in addition to mercurial exposure...It is noteworthy that many vaccines and sera contain small amounts of mercury as preservatives which are injected together with the biologic material. These small amounts of mercurial compounds, which enter the body unnoticed, could act as sensitizing substances. This fact should be kept in mind in the analysis of future cases of acrodynia.*[43]

Engley reported in 1956 that in tissue culture experiments evaluating the toxicity of mercury, it has been shown that Thimerosal was more toxic that other mercurials such as mercurochrome, phenylmercuric nitrate, mercuric chloride, mercresin, and mercuric cyanide, among others.[44] Specifically, Engley stated [emphasis added]:

> *The technique used here consisted of the following: Serial dilutions of the chemicals under test were prepared in embryonic extract as shown in Figure 9. Thin slices of human skin were removed with sterile instruments and the tissue cut into fragments approximately 2mm square (Figure 1). Each explant was placed on a cover slip in plasma, and embryonic extract containing the drug dilutions was added. The tissue was centered on the cover slip and after a clot forms, the preparation was sealed onto a depression slide and incubated at 37°C for eight to ten days. Cultures were examined microscopically for growth at daily intervals and compared in growth with control skin tissue...Graph 15 compares mercurial compounds and shows how they fit in with other compounds in*

---

[42] Exhibit ELI - 1064, Letter of July 22, 1935 From Dreictor Biological Laboratories of Pitman – Moore Company to W. A. Jamieson, Director, Biological Division, Eli Lilly & Company.
Subcommittee on Human Rights and Wellness, Government Reform Committee. Mercury in Medicine Report. Washington, DC: Congressional Record, May 21, 2003;E1011-30.
[43] Warkany J, Hubbard DM. Acrodynia and Mercury. J Pediatr 1953;42:365-386.
[44] Engley FB. Mercurials as disinfectants. Soap and Chemical Specialties 1956;200-5, 223-5.

toxicity...Mercurochrome appears to be the least toxic ranging down through Merthiolate.

In addition, Engley reported that Thimerosal and other mercury-containing preservatives were not effective to reduce bacterial contamination. Specifically, Engley stated [emphasis added]:

The use of mercurials as preservatives in vaccines and antisera is of considerable interest. These chemicals are added to protect against the introduction of organisms in multi-use containers in particular. We have always wondered about their efficacy in that both vaccines and antisera contain reactive groups to tie up these compounds. In a series of continuing experiments of the past several years we have begun to evaluate various preservatives in serum and vaccines under conditions of use. Employing stock vaccines and serum with and without preservatives and stored at varying lengths of time a contaminating dose of representative sporeformer (Bacillus subtilis) in the spore stage gram negative rod (E. coli) and gram positive coccus (S. aureus) were added. While the mercurial preservatives had good activity on initial addition, after storage of three, six or more months decreasingly less negligible residual activity appeared to be left, indicating that the chemical was tied up by the protein of the biological or otherwise inactivated. ***A check on a series of over one thousand bottles of various biologicals from clinics obtained after use revealed that up to five percent contained microorganisms. This would suggest that once these biologicals are in the hands of users a problem still exits.***

Nelson and Gottshall from the Division of Biologic Products, Bureaus of Laboratories, Michigan Department of Public Health published in 1967 [emphasis added]:

Pertussis vaccines preserved with 0.01% Merthiolate are more toxic for mice than unpreserved vaccines prepared from the same parent concentrate and containing the same number of organisms*...An increase in mortality was observed when Merthiolate was injected separately, before or after an unpreserved saline suspension of pertussis vaccine.*[45]

On September 7, 1971, **Dr. Smith, the Head of the Biological Regulatory Requirements at Eli Lilly and Company sent a letter to Dr. Sigel, Professor of Microbiology at the University of Miami School of Medicine stating that levels 100-fold lower of Thimersoal (Merthiolate) than those present in vaccine formulations were toxic to tissue culture cells.** Specifically this letter stated.

Pursuant to our telephone conversation of September 1, 1971, we are sending today, under separate cover and packed with a refrigerant, a 1 10 mL. sample of Mumps Virus Inactivated, Lot No. L-01159, and a 1 10 mL. sample of Influenza Virus Vaccine, Bivalent, Lot No. L-01160. ***Both samples contain***

[45] Nelson EA, Gottshall RY. Enhanced Toxicity for Mice of Pertussis Vaccines When Preserved with Merthiolate. Appl Microbiol 1967;15:590-593.

MERTHIOLATE as a preservative in a final concentration of 1/10,000 which, for your information, could be toxic for tissue cells, lymphocytes, etc. Therefore, you may need to dialyze these samples prior to use depending upon your test system. We have found that for tissue culture work, the MERTHIOLATE must be in a concentration of less than 1/1,000,000 in order not to be toxic to the tissue cells.[40]

Axton, from the University of Rhodesia, reported in 1972 on six cases of poisoning after injection of Merthiolate. The author reported:

> *The case histories of four children and two adults who were accidentally given toxic amounts of Merthiolate are recorded...Five out of the six patients died...*[41]

Jones reported in 1973 on the danger of skin burns from the interaction between Thimerosal and aluminum. The authors stated:

> *It is believed that the lesion suffered by the patient was a burn produced by heat generated by the action of Thiomseral on aluminum. The active ingredient in Thiomersal is sodium o-(ethylmercurithio)-benzoate, which has a high mercury content. Mercury is known to act as a catalyst and to cause aluminum to oxidize rapidly, with the production of heat.*[48]

In 1973, it was reported that Merthiolate (Thimerosal) reacted with aluminum adversely to produce heat and corrosion Specifically, it was reported [emphasis added]:

> *Certain chemicals used in operating rooms will react with aluminum, releasing heat or caustic products that could cause the patient burns...A report in the literature (H.T. Jones, Danger of skin burns from Thimerosal, British Medical Journal, Vol. 2, page 504, 1972) describes a clinical incident in which a patient was burned when Thimerosal (Tincuture of Merthiolate, Lilly) was used as a skin preparation prior to electrosurgery utilizing a disposable aluminum return plate electrode. The indication is that other mercury-containing compounds may cause similar reactions. We evaluated the effect of Tincture of Merthiolate on four foil-clad cardboard disposable return electrodes, as well as on the Ritter Chick-It Dispersive Plate...No reaction was evident with the Ritter copper foil electrode or the stainless steel reusable plate. Neither temperature rise nor corrosion was noted on these electrodes. All of the aluminum foil samples, however, were severely corroded, and the peak temperatures recorded are shown in the table...**Because of the heat generated by the chemical reaction of Merthiolate***

---

[40] Exhibit ELI 643, A September 7, 1971 Letter from Dr. Smith, Head of Biological Regulatory Requirements at Eli Lilly and Company to Dr. Sigel, Professor of Microbiology at the University of Miami School of Medicine

[41] Axton JHM. Six cases of poisoning after a parenteral organic mercurial compound (Merthiolate). Postgrad Med J 1972;48:417-21.

[48] Jones HT. Dangers of skin burns from Thiomersal. Br Med J 1972;2:504-5.

and aluminum, and because of the corrosion of the aluminum...hospitals should not use mercury-containing liquids in conjunction with aluminum...[49]

Gassett et al. in 1975 examined mercury distribution following administration of thimerosal to animals. They stated [emphasis added]:

A comparison of topical and subcutaneous administration of thimerosal to rabbits shows that a substantial concentration of mercury was present in blood and tissues of the treated animals and their offspring. ***Thimerosal was found to cross the blood-brain and placenta barriers.***[50]

In 1975, Blair et al. examined mercury distribution and form following administration of thimerosal to animals. The authors reported [emphasis added]:

Squirrel monkeys were dosed intranasally with saline or thiomersal (sodium ethylmercurithiosalicylate, 0.002 percent w/v) daily for six months. The total amounts of thiomersal given during the six months period were 418 mug (low dose group) and 2280 mug (high dose group). This was equivalent to 207 and 1125 mug mercury. The dose differential was achieved by more frequent administration to the high dose group. Mercury concentrations were significantly raised over control values in brain (high dose group only), liver, muscle and kidney, but not in blood. Concentrations were highest in the kidney, moderate in liver and lowest in brain and muscle. Much of the mercury was present in the inorganic form (37-91 percent). No evidence of toxicity due to thiomersal was seen in any animal. ***Nevertheless accumulation of mercury from chronic use of thiomersal-preserved medicines is viewed as a potential health hazard for man.***[51]

In 1977, Fagan et al. reported, in a study funded by the National Institute of Environmental Health Sciences, that between 1969 and 1975 there were 13 cases of exomphalos treated by Thimerosal. The authors determined that 10 of the patients had died, and there tissues were analyzed for mercury content. The researchers stated [emphasis added]:

The results showed that Thimerosal can induce blood and organ levels of organic mercury which are well in excess of the minimum toxic levels in adults and fetuses...Although Thiomersal is an ethyl mercury compound, it has similar toxicological properties to methyl mercury and the long-term neurological sequelae produced by the ingestion of either methyl or ethyl mercury-based fungicides are indistinguishable.

[49] Hazard: Merthiolate and Aluminum Electrodes. Health Devices. September 1973, pgs. 271-272.
[50] Gasset AR, Iloi M, Ishii Y, Ramer RM. Teratogenicities of ophthalmic drugs. II. Teratogenicities and tissue accumulation of thimerosal. Arch Ophthalmol 1975;93:52-55.
[51] Blair AM,N, Clark B, Clarke AJ, Wood P. Tissue concentrations of mercury after chronic dosing of squirrel monkeys with thiomersal. Toxicology 1975;3:171-6.

The authors also concluded the fact that mercury readily penetrates intact membranes and is highly toxic seems to have been forgotten, and that equally effective and far less toxic broad-spectrum antifungal and antibacterial antiseptics are currently available.[52]

Heyworth and Truelove stated in 1979 [emphasis added]:

> *For many years, Merthiolate was known to have anti-microbial activity. When it was first introduced as an anti-microbial preservative, little information about the fundamental biological effects of organic mercury compounds was available. We* ***should like to suggest that Merthiolate should now be regarded as an inappropriate preservative for anti-lymphocytic globulin preparations and other materials which are intended for administration to human subjects.***[53]

In 1974, the FDA undertook a comprehensive review of the safety and effectiveness of over-the-counter (OTC) medicines. As one facet of this review, a panel of experts was assembled to review the safety and efficacy of OTC drugs containing mercury. The Advisory Review Panel on OTC Miscellaneous External Drug Products began its review in 1975. In 1980, the panel delivered its report to the FDA. It reviewed 18 products containing mercury, and found them all either unsafe or ineffective for their stated purpose of killing bacteria to prevent infections. In terms of effectiveness, the panel stated that, "mercury compounds as a class are of dubious value for anti-microbial use." They stated that, "mercury inhibits the growth of bacteria, but does not act swiftly to kill them" In fact, the panel cited a 1935 study of the effectiveness of Thimerosal in killing staphylococcus bacteria on chick heart tissue. The study determined that Thimerosal was **35-times more toxic to the heart tissue it was meant to protect than the bacteria it was meant to kill.** In terms of safety, the panel cited a number of studies demonstrating the highly allergenic nature of Thimerosal and related organic mercury products. For instance, they cited a Swedish study that showed that 10 percent of school children, 16 percent of military recruits, and 18 percent of twins, and 26 percent of medical students had hypersensitivity to Thimerosal. They stated that while organic mercury compounds like Thimerosal were initially developed to decreased the toxicity of the mercury ion, Thimerosal was actually found to be more toxic than bichloride of mercury for certain human cells. By way of summary, the stated, "The Panel concludes that Thimerosal is not safety for OTC topical use because of its potential for cell damage of applied to broken skin, and its allergy potential. It is not effective as a topical antimicrobial because its bacteriostatic action can be reversed."[54]

Forstrom et al. published in 1980:

---

[52] Fagan DG, Pritchard JS, Clarkson TW, Greenwood MR. Organ Mercury Levels in Infants with Omphaloceles Treated with Organic Mercurial Antiseptic. Arch Dis Child 1977;52:962-964.
[53] Heyworth MF, Truelove SC. Problems Associated with the use of Merthiolate as a Preservative in Anti-Lymphocytic Globulin. Toxicology 1979;12:325-333.
[54] Subcommittee on Human Rights and Wellness, Government Reform Committee, Mercury in Medicine Report, Washington, DC: Congressional Record, May 21, 2003:E1011-30.

> *...reactions can be expected in such a high percentage of Merthiolate-sensitive persons that Merthiolate in vaccines should be replaced by another antibacterial agent.*[55]

In 1983, Kravchenko et al. published [emphasis added]:

> *Thus Thimerosal, commonly used as a preservative, has been found not only to render its primary toxic effect, but also is capable of changing the properties of cells.* ***This fact suggests that the use of Thimerosal for the preservation of medical biological preparations, especially those intended for children, is inadmissible.***[56]

Crook and Freeman in 1983 reported on reactions induced by the concurrent use of Thimerosal and antibiotics. The authors reported [emphasis added]:

> *The evidence points to an interaction between Thimerosal and tetracycline...We investigated the interaction between Thimerosal and tetracycline by administering these drugs to rabbits. No other preservative or disinfectants were added. Thus, the response observed (Table 1) appears to be due to an interaction between Thimerosal and tetracycline...* ***The reaction that develops in both animals and humans appears to be due to an interaction between Thimerosal and tetracyclines.***[57]

It was reported in 1983 that administration of aqueous Merthiolate (Thimerosal) resulted in a child dieing from mercury toxicity.[58] The article stated [emphasis added]:

> *The Ohio Board of Pharmacy has received an investigative report from the Ohio Department of Health's Division of Epidemiology regarding the death of a 21-month old child due to mercury poisoning.* ***The investigation strongly implicated the Thimerosal solution as 'the source of mercury that subsequently resulted in the child's death' since no other source could be identified.*** *The poisoning apparently resulted from the improper use of Thimerosal Topical Solution, U.S.P. (1:1000), prescribed by a physician for the treatment of chronic otitis media.*

In 1984, Royhans et al. reported on mercury toxicity following pediatric Thimerosal (Merthiolate) ear irrigations.[59] The researchers stated [emphasis added]:

---

[55] Forstrom L, Hannuksela M, Kousa M, Lahmuskallio E. Merthiolate Hypersensitivity and Vaccination. Contact Dermatitis 1980;6:241-245.
[56] Kravchenko AT, Dzagurov SG, Chervonskaia GP. Evaluation of the Toxic Action of Prophylactic and Therapeutic Preparations on Cell Cultures Paper III: The Detection of Toxic Properties in Medical Biological Preparations by the Degree of Cell Damage in the L-132 Continuous Cell-Line. Zh Mikrobiol' Epidemiol Immunobiol 1983;3:87-92.
[57] Crook TG, Freeman JJ. Reactions induced by the concurrent use of thimerosal and tetracycline. Am J Optom Physiol Opt 1983;60:759-61.
[58] Mercury poisoning in child treated with aqueous merthiolate. Md State Med J 1983;32:523.
[59] Rohyans J, Walson PD, Wood GA, MacDonald WA. Mercury toxicity following merthiolate ear irrigations. J Pediatr 1984;104:311-3.

*Although aqueous merthiolate has been used for years as a topical antiseptic, a recent review of its use by the Food and Drug Administration resulted in its classification as 'less than effective.' Furthermore, two of the ingredients (thimerosal and borate) in merthiolate are toxic if absorbed or injected...**Symptoms of organic mercury poisoning chiefly involve the central nervous system, including paresthesia of the mouth, lips, tongue, and extremities; speech disorders, with difficulty in articulating words; difficulty in swallowing; salivation; neurasthenia; inability to recall basic information; emotional instability; ataxia; clumsiness; stupor; and coma...Reactions to mercury depend to a large extent on the form of the chemical agent; its absorption, storage, and excretion; duration of exposure; and individual susceptibility.** Both inorganic and dissociable organic mercurials appear to act by the same mechanism. Mercury ion reacts with sulfhydryl groups to form mercaptides, which inactivate sulfhydryl enzymes and interfere with cellular metabolism...*

*The blood-brain barrier, is also more permeable to organic than inorganic mercury. **There are definite individual differences in sensitivity to the effects of mercurials. Some patients tolerate prolonged exposure without symptoms; others have significant systemic signs and neurological disability with much less exposure. The mercury in Merthiolate is a thiosalicylate compound that is converted to inorganic mercury more rapidly than is methyl mercury. The organic compound itself is also easily absorbable, and undergoes widespread tissue distribution. Toxicity may be related both to the biotransformation into inorganic mercury and to the unchanged compound, both of which cause degenerative changes in the brain, especially in the visual cortex and cerebellum, and proliferative changes throughout the cerebellar context.***

Winship reported in 1985:

Multi-dose vaccines and allergy-testing extracts contain a mercurial preservative, usually 0.01% Thimerosal, and may present problems occasionally in practice. It is, therefore, now accepted that multi-dose injection preparations are undesirable and that preservatives should not be present in unit-dose preparations.[60]

Stetler et al. [one of the co-authors is Dr. Walter Orenstein who was latter to become Director of the National Immunization Program (NIP), CDC] from the CDC evaluated the use of Thimerosal as a preservative in vaccines in 1985. The authors reported that Thimerosal was ineffective as a vaccine preservative, and that giving more mercury than was present in a single Thimerosal-containing vaccine might pose a health hazard to vaccine recipients. Specifically, the authors stated regarding the effectiveness of Thimerosal as a preservative in vaccines [emphasis added]:

[60] Winship KA. Organic Mercury Compounds and Their Toxicity. Adv Drug React Ac Pois Rev 1986;3:141-180.

> *Laboratory experiments in this investigation have shown up to 2 weeks' survival of at least one strain of group A Streptococcus in multidose DTP [Diphtheria-Tetanus-Pertussis] vials. The manufacturer's preservative effectiveness tests showed that at 4°C, 4.5% of the challenge Streptococcus survived 14 days after inoculation into a multi-dose DTP vaccine vial.* ***At currently used concentrations, Thimerosal is not an ideal preservative.***

The authors also warned regarding the toxicity of Thimerosal [emphasis added]:

> *However, because Thimerosal is an organic mercurial compound, higher concentrations might reduce vaccine potency* ***or pose a health hazard to recipients*** *[i.e. It should be noted that the dose of Thimerosal was not increased in a given vial of vaccine, but beginning in the early 1990s the amount of Thimerosal children received approximately tripled, because 3 Thimerosal-containing vaccines were given on one day to infants with the addition of the hepatitis B and Hib vaccines to the routine childhood immunization schedule, and hence it was as though the amount of Thimerosal in a given vial increased approximately 3-fold.]*

The authors also made the following calculations and recommendations regarding the use of multi-dose vials with a Thimerosal preservative:

> *Single-unit packaging would approximately double the cost of DTP per dose. For example, one manufacturer charges $5.12 for a 15-dose vial of DTP vaccine or $0.34, per dose. If the $0.20 cost of a disposable syringe are added, the total cost per dose to the physician would be about $0.54. The same manufacturer charges $10.40 for a package of ten single DTP doses (needle and syringe pre-packed) or $1.04 per dose... Given the prices mentioned above and the fact that approximately 18 million doses of DTP are administered each year, the cost of switching to single-dose packing might be approximately $9 million. Neither research to develop a better preservative nor recommendations to consider single-dose packaging appear to be warranted... The Thimerosal preservative present in DTP vaccine requires substantial time to kill organisms and cannot be relied upon to prevent transmission of bacteria under conditions of practice when a vial is used over a short period. Instead, the most important means of preventing abscesses secondary to DTP vaccination is to prevent contamination by careful attention to sterile technique.*[61]

Cox and Forsyth recommended in 1988:

> *However, severe reactions to Thimerosal demonstrate a need for vaccines with an alternative preservative.*[62]

---

[61] Stetler HC, Garbe PL, Swyer DM, Facklam RR, Orenstein WA, West GR, Dudley J, Bloch AB. Outbreaks of Group A Streptococcal Abscesses Following Diphtheria-Tetanus Toxoid-Pertussis Vaccination Pediatrics 1985;75:299-303.

[62] Cox NH, Forsyth A. Thiomersal Allergy and Vaccination Reactions. Contact Dermatitis 1988;18:229-233

Nascimento et al. reported in 1990 on a death following Thimerosal ingestion. Specifically, it was:

> *A case of mercurial poisoning caused by ingestion of an organic mercurial compound, thimerosal, found in local antiseptic solutions. The clinical picture consisted of grave neurological symptoms which were not reversed by penicillamine and resin administration despite rapid plasma level reduction of mercury. We call attention to this case because of the widespread availability of antiseptic solutions containing mercurial compounds...*[63]

In 1991, Seal et al. published [emphasis added]:

> ***Thimerosal is a weak antibacterial agent that is rapidly broken down to products, including ethylmercury residues, which are neurotoxic.*** *Its role as a preservative in vaccines has been questioned, and the pharmaceutical industry considers its use as historical.*[64]

In 1991, Maurice R. Hilleman sent a Merck internal correspondence to Dr. Gordon Douglas on the Vaccine Task Force Assignment Thimerosal (Merthiolate) Preservative – Problems, Analysis, Suggestions for Resolution. It was stated in this document [emphasis added]:

> *PROBLEM: The regulatory control agencies in some countries, particularly Scandinavia (especially Sweden), but also U.K., Japan, and Switzerland, have expressed concern for thimerosal, a mercurial preservative, in vaccines...PUTTING THIS INTO PERSPECTIVE: For Babies:* ***The 25 ug of mercury in a single 0.5 mL dose and extrapolated to a 6 lb. baby would be 25X the adjusted Swedish daily allowance of 1.0 ug for a baby of that size.*** *The total mercury burden in a baby is unknown but it has been stated that the blood level of a newborn may exceed that of the mother.* ***If 8 doses of thimerosal-containing vaccine were given in the first 6 months of life (3 DPT, 2 HIB, and 3 Hepatitis B) 200 ug of mercury given, say to an average size of 12 lbs., would be about 87X the Swedish daily allowance of 2.3 ug of mercury for a baby of that size. When viewed in this way, the mercury load appears rather large.***[65]

On September 1, 1993, Lilly prepared a Material Safety Data Sheet (MSDS) for Thimerosal. It stated [emphasis added]:

> *SECTION 5 - HEALTH HAZARD INFORMATION: CALIFORNIA PROPOSITION 65 WARNING.* ***WARNING: This product contains a chemical***

---

[63] Nascimento I.O. Lorenzi Filho G. Rocha Ados S. Lethal mercury poisoning due to ingestion of merthiolate. Rev Hosp Clin Fac Med Sao Paulo 1990;45:216-8.
[64] Seal D. Ficker L. Wright P. Andrews V. The Case Against Thimerosal. Lancet 1991;338:315-316.
[65] Exhibit MRK 286. From Maurice R. Hilleman to Dr. Gordon Douglas. Vaccine Task Force Assignment Thimerosal (Merthiolate) Preservative – Problems, Analysis, Suggestions for Resolution. March 27, 1991.

> *known to the State of California to cause birth defects or other reproductive harm. Human Occupational: Effects, Including Signs and Symptoms, of Exposure...* ***Exposure to mercury in utero and in children may cause mild to severe mental retardation and mild to severe motor coordination impairment...*** *Animal Toxicity Data Repeat Exposure...* ***Reproduction/Developmental: Thimerosal – Increased abortion and fetal death, no malformations. Mercury causes nervous system effects including mild to severe mental retardation and motor coordination impairment...*** *SECTION 6 EMERGENCY AND FIRST AID PROCEDURES:* ***Ingestion: Call a physician or poison control center...Use of chelating agents such as BAL may be needed to treat ingestion of mercury. Immediately transport to a medical care facility and see a physician.***[66]

In 1996, Lowell et al., from the Washington University School of Medicine, stated [emphasis added]:

> *Preparations of HBIG [hepatitis B immunoglobulin] use thimerosal (a mercury derivative) as a preservative.* ***We encountered mercury toxicity, in a patient who received high-dose immunoprophylaxis...HBIG preparations contain thimerosal as a preservative, which contains 49% organically bound mercury. Previous reports have demonstrated that administration of thimerosal-containing products may lead to mercury poisoning.*** *Various forms of chelation have been used to treat mercury poisoning; our patient had an excellent response to DMSA. No DMSA toxicity was noted, and neurological recovery was complete.* ***Physicians should suspect mercury toxicity in patients receiving high-dose HBIG.***[67]

In August of 1998, an FDA internal "Point Paper" was prepared for the Maternal Immunization Working Group. This document recommended [emphasis added]:

> *For investigational vaccines indicated for maternal immunization, the use of single dose vials should be required to avoid the need of preservative in multi-dose vials...* ***Of concern here is the potential neurotoxic effect of mercury especially when considering cumulative doses of this component in early infancy.***[68]

In 1997, Congress passed and the President signed into law, the Good and Drug Administration Modernization Act (FDAMA). Among other things, this law required the FDA to compile a list of foods and drugs that contained intentionally-introduced mercury, study its effects on the human body, and restrict its use if found to be harmful.[69]

---

[66] Thimerosal, Material Safety Data Sheet – Lilly, Revised September 1, 1993.
[67] Lowell JA, Burgess S, Shenoy S, Peters M, Howard TK. Mercury poisoning associated with hepatitis-B immunoglobulin. Lancet 1996;347:480.
[68] Subcommittee on Human Rights and Wellness, Government Reform Committee. Mercury in Medicine Report. Washington, DC: Congressional Record, May 21, 2003:E1011-30.
[69] Subcommittee on Human Rights and Wellness, Government Reform Committee. Mercury in Medicine Report. Washington, DC: Congressional Record, May 21, 2003:E1011-30.

The task of analyzing the amount of mercury in vaccines and its ramifications was assigned to Dr. Leslie Ball, a pediatrician employed at the FDA, and her husband and colleague Dr. Robert Ball, a medical office at FDA's Center for Biological Evaluation and Research (CBER). The pair developed two working conclusions following their review: (1) The recommended guidelines for exposure to methylmercury were a good starting point for reviewing exposure to ethylmercury; and (2) the amount of ethylmercury in children's vaccines exceeded the EPA's guidelines for exposure to methylmercury. An exchange of e-mails in October of 1998 makes clear that Dr. Leslie Ball was already leaning toward the removal of Thimerosal from vaccines. It also makes clear that there was internal resistance to such an action. Dr. Marion Gruber of the Office of Vaccine Research and Review forwarded an internal memo to Dr. Ball, which concluded, "...no scientific data to take regulatory actions and to recommend to take Thimerosal either out of vaccines or to leave it in." Dr. Ball's response on October 15, 1998 was sharp, "I disagree about the conclusion regarding no basis for removal of Thimerosal...However, there are factors/data that would argue for the removal of Thimerosal, including data on methylmercury exposure in infants and the knowledge that Thimerosal is not an essential component to vaccines. In addition, the European community is moving to ban Thimerosal."[70]

An important part of the FDA's review was a comparison of the amount of ethylmercury in vaccines to the recommended safe levels for exposure to methylmercury established by the EPA and the FDA. In 1999 (June 28, 1999), a consultant to the FDA, Dr. Barry Rumack, developed a pharmacokinetic model to analyze the amount of mercury to which infants were being exposed. The charts developed by Dr. Barry Rumack demonstrated that most children in the 1990s received doses of ethylmercury in their vaccines that exceeded the EPA's limits for exposure to methylmercury (0.1 micrograms per kilogram per day) for at least the first six months of their lives. Even more significantly, the charts also indicated that most children received doses of ethylmercury that exceeded the FDA's less-restrictive limits (0.4 micrograms per kilogram per day) for at least the first two months of their lives. It is noteworthy that the charts produced by Dr. Rumack, and the FDA's analysis in general, failed to take into consideration background levels of mercury to which children were exposed from other sources. Dr. Ball pointed out this weakness in her June 1999 email, "These calculations do not account for other sources of Hg [mercury] in the environment. Even infants can have additional exposures, e.g. breast milk." One document written by Dr. Ball estimated that exposure to mercury from other sources than vaccines could total roughly 80 to 100 micrograms per year. Background levels were included in all calculations prepared the European Medical Evaluation Agency (EMEA), which was at the time reviewing Thimerosal in vaccines in Europe.[71]

In mid-June of 1999, CBER's findings came to the attention of Dr. Neal Halsey, Director of the Johns Hopkins Institute for Vaccine Safety. Halsey is a pediatrician and highly

[70] Subcommittee on Human Rights and Wellness, Government Reform Committee. Mercury in Medicine Report. Washington, DC: Congressional Record, May 21, 2003:E1011-30.
[71] Subcommittee on Human Rights and Wellness, Government Reform Committee. Mercury in Medicine Report. Washington, DC: Congressional Record, May 21, 2003;E1011-30.

respected vaccine expert. When he learned of the CBER findings, he was finishing up a four-year term as chairperson of the AAP Committee on Infectious Diseases, the committee that determines AAP vaccination policy and edits the *Red Book*. Long before he heard about the Thimerosal findings, Halsey had become worried about the progress of vaccination protest groups in the United States. In May, Congress had held a contentious hearing on the dangers of vaccination. Halsey feared that the tide was turning against childhood vaccination, with potentially dangerous consequences. Halsey confirmed CBER's calculations and did his own research on mercury, consulting with experts around the country. He became convinced that the findings were worthy of alarm, and her worried if they became public prematurely, vaccination protesters would use them to stage yet another attack on the nation's immunization programs. Halsey met with officials as CBER on June 22nd and then called Dr. Walter Orenstein, director of the CDC's NIP.[72]

The next day, on June 23, 1999, Dr. Halsey wrote a letter to the members of the AAP's Committee on Infectious Diseases that stated [emphasis added], "**In the past few days, I have become aware that the amount of Thimerosal in most hepatitis B, DTaP and Hib vaccines that we administer to infants results in a total dose of mercury that exceeds the maximum exposure recommended by the EPA, the FDA, CDC, and WHO...**"[73]

The EMEA, which is responsible for establishing guidelines for the use of drugs and biologics in the European Union, issued a report on June 29, 1999, following an initial meeting in London on April 19, 1999 encouraging the removal of Thimerosal from childhood vaccines [emphasis added]:

> *Vaccines: The fact that the target population for vaccines in primary immunization schedules is a health one, and* ***in view of the demonstrated risks of Thimerosal and other mercurial containing preservatives****, precautionary measures (as outlines below) could be considered...For vaccination in infants and toddlers, the use of vaccines without Thimerosal and other mercurial preservatives should be encouraged.*[74]

On June 29, 1999, SmithKline Beecham Pharmaceuticals internally distributed a report evaluating thimerosal toxicity. It stated [emphasis added]:

> ***The toxicity profile of ethylmercury would appear to be similar to that of methylmercury****. Therefore, data on methylmercury have been used in the assessment of risks associated with ethylmercury...The fact that the target population for vaccines in primary immunization schedules is a health one, and in*

[72] Shaw FE (ed). *Hepatitis Control Report - Uproar over a little-known preservative, Thimerosal, jostles U.S. hepatitis B vaccination policy.* Summer 1999, Volume 4, Issue 2.
[73] Subcommittee on Human Rights and Wellness, Government Reform Committee. Mercury in Medicine Report. Washington, DC: Congressional Record, May 21, 2003:E1011-30.
[74] Subcommittee on Human Rights and Wellness, Government Reform Committee. Mercury in Medicine Report. Washington, DC: Congressional Record, May 21, 2003:E1011-30.

> ***view of the demonstrated risks of Thimerosal and other mercurial containing preservatives, precautionary measures (as outlines below) could be considered***[75]

On June 30th, NIP staff flew to Washington to meet with FDA, AAP, and vaccine manufacturers. From the start Halsey and his colleagues at AAP, including the new chairperson of the Infectious Disease Committee, Dr. Jon Abramson, took a strong proactive stance. They argued that physicians should be told-soon-about the amount of mercury in vaccines and the conflict with a federal guideline. CDC was surprised by the urgent and undoubting position taken by Halsey and his colleagues at AAP. CDC officials argued that there was no need for precipitous actions. They were loath to undermine confidence in existing vaccines by labeling some vaccines "bad" (Thimerosal-containing) and "good" (Thimerosal-free). But, in further discussions through the first few days of July, it became clear that Halsey and AAP would not retreat-they believed that immediate action was needed.[76]

There was tremendous reluctance on the part of some officials to admit that a mistake had been made in allowing ethylmercury to be used in vaccines. However, the institutional resistance to change was counter-balanced by the growing realization that there was more ethylmercury in childhood vaccines than previously thought, and that nobody had thought to calculate the cumulative amounts. The essence of the debate was captured in a 1999 e-mail from a former FDA official weighing the pros and cons of taking action. He opined that hastening the removal of Thimerosal from vaccines would [emphasis added]:

> *...**raise questions about FDA being 'asleep at the switch' for decades by allowing a potentially hazardous compound to remain in many childhood vaccines, and not forcing manufacturers to exclude it from new products.** It will also raise questions about various advisory bodies regarding aggressive recommendations for use. (We must keep in mind that the dose of ethylmercury was not generated by 'rocket science'. Conversion of the percentage Thimerosal to actual micrograms involves ninth grade algebra. What took the FDA so long to do the calculations? Why didn't CDC and the advisory bodies do these calculations when they rapidly expanded the childhood immunization schedule?)"*[77]

Similarly, in a July 2, 1999, email, Dr. Ruth Etzel of the Department of Agriculture also noted [emphasis added]:

> *We must follow three basic rules: **(1) act quickly to inform pediatricians that the products have more mercury than we realized; (2) be open with consumers about why we didn't catch this earlier; (3) show contrition.** As you know, the Public Health Service informed us yesterday that they were planning to conduct business as usual, and would probably indicate no preference for either product.*

---

[75] Plaintiff's Exhibit MISC – 174. Fax From Anne P. Walsh to Scott Harward on 6/29/99.
[76] Shaw FE (ed). *Hepatitis Control Report - Uproar over a little-known preservative, Thimerosal, jostles U.S. hepatitis B vaccination policy.* Summer 1999, Volume 4, Issue 2.
[77] Subcommittee on Human Rights and Wellness, Government Reform Committee. Mercury in Medicine Report. Washington, DC: Congressional Record, May 21, 2003:E1071-50.

While the Public Health Service may think that their 'product' is immunizations, I think their 'product' is their recommendations. If the public loses faith in the Public Health Services recommendations, then the immunization battle will falter. To keep faith, we must be open and honest and move forward quickly to replace these products.[78]

Within AAP, the issue ascended quickly from Halsey's committee to the executive board. **AAP executives felt that their members needed more than just information about Thimerosal-they also needed a way to reduce mercury exposure in their tiny patients. They feared that pediatricians who continued to administer Thimerosal-containing vaccines could face a flurry of lawsuits, perhaps claiming that children had acquired learning disabilities from mercury exposure.**[79]

Negotiations continued with AAP nearly around the clock. Everyone was becoming exhausted. As the groups continued negotiations over days, worries increased that the story would leak to the press in an uncontrolled way, triggering a general vaccination scare. "Everyone worried that, with the vaccination protest groups looking over our shoulders, if they got the sense that some [toxicological] standard was broken, all hell would break loose," said a senior official who worked on the issue. Finally, after a week of late night meetings involving the AAP executive board, Surgeon General Dr. David Satcher, CDC Director Dr. Jeffrey Koplan and other CDC officials, FDA, the manufacturers, and others, the exhausted group, struck a compromise. An AAP-USPHS joint statement was issued on July 7 at 4:15 PM.[80]

Dr. Johns Clements, a physician from the World Health Organization (WHO) said at the NIH workshop regarding the United States' policy of removing Thimerosal from vaccines, "the U.S. has gone on its due course to identify a problem and correct it. But there is a knock-on effect which the world must bear as a consequence." Clements pointed out that only multi-dose, multi-puncture vials can be used in developing countries because of cost and cold-chain considerations. Removing Thimerosal from these vials is not an option for WHO, at least for the next several years, he said. In an August interview, Dr. Halsey defended the Thimerosal decision-making process used by AAP and CDC. It would not have been possible to deal with Thimerosal in the usual public forums like Advisory Committee on Immunization Practices (ACIP), Halsey said, because the presence of vaccination protestors would have made rational discussion hopeless. Deliberations were handled in the only way possible he said. But Halsey acknowledged that many of his immunization colleagues are angry with him and miffed about the way the issue was handled.[81]

---

[78] Subcommittee on Human Rights and Wellness, Government Reform Committee. Mercury in Medicine Report. Washington, DC: Congressional Record, May 21, 2003:E1011-30.
[79] Shaw FE (ed). *Hepatitis Control Report - Uproar over a little-known preservative, Thimerosal, jostles U.S. hepatitis B vaccination policy.* Summer 1999, Volume 4, Issue 2.
[80] Shaw FE (ed). *Hepatitis Control Report - Uproar over a little-known preservative, Thimerosal, jostles U.S. hepatitis B vaccination policy.* Summer 1999, Volume 4, Issue 2..
[81] Shaw FE (ed). *Hepatitis Control Report - Uproar over a little-known preservative, Thimerosal, jostles U.S. hepatitis B vaccination policy.* Summer 1999, Volume 4, Issue 2..

The joint statement that was released on July 7, 1999 by the AAP and the USPHS included the following points: (1) acknowledged that some children may have been exposed to levels of mercury that exceed one Federal guideline on methylmercury during the first six months of life; (2) asserted there is no evidence of any harm caused by Thimerosal in vaccines; (3) called on vaccine manufacturers to make a clear commitment to reduce as expeditiously as possible, the mercury content of their vaccines; (4) urged doctors and parents to immunize all children, even if Thimerosal-free vaccines were not available; and (5) encouraged doctors and parents to postpone the hepatitis B vaccine (which contained Thimerosal at the time, and was generally given immediately after birth) until the child was two to six months old, unless the mother tested positive for hepatitis B.[82]

Subsequent to the July 7, 1999 recommendation to remove Thimerosal from vaccines, a meeting from August 11-12, 1999 was held by the United States Public Health Service and CDC, "The National Vaccine Advisory Committee Sponsored Workshop on Thimerosal Vaccines" at the National Institute of Health, Lister Hill Auditorium, Bethesda, Maryland. Among those in attendance including representatives from FDA, CDC, Merck, North American Vaccine, Pfizer, SmithKline Beecham, Wyeth-Lederle Vaccine, and Pasteur Mericux Connaught. The following are a few excerpts from the official transcript that was kept for the meeting [emphasis added]:

Dr. William Egan (FDA): Pages 25-26: *In the past, it was thought that single-dose containers, like multi-dose containers, should contain preservatives, the rationale being that the addition of a preservative during the manufacturing process or during the filling operation served to help ensure that the product was free of microbial agents and their toxins. In deed, at the International Symposium on Preservatives in Biological Products held 25 years age, in San Francisco · This was under the auspices of the IABS Dr. Edward Seligman, JR., at the time the Director of the Bureau of Biologics Division of Product Quality Control, had the following comment: 'Because of the numerous complex processing stages in the manufacture of biological products, good manufacturing procedures include the addition of preservatives early in the manufacture of many types of products to aid in preventing contamination during production. Even if products are sterilized by filtration prior to filling into final containers, contamination during earlier stages can result in soluble products that alter the purity of the product, increase toxicity, and result in pyrogens, all of which cannot be removed without alteration of the product itself.' Now today, GMPs are viewed differently, and it would be argued that a well-controlled process does not require the addition of a preservative to ensure sterility. However, I think at this point, its worthwhile noting that sterility is not an absolute term. Sterility does not mean zero microbial organisms in one hundred percent of the containers. Let me show some data that was presented in Germany at this symposium 25 years ago. Well, this is filling data, so number of lots that were filled and the percentage of non-sterile filling lots. And with no preservatives in ampules, 5.6 percent of the lots were found to be non-sterile. This is using the test that's in the CFR. For multi-dose containers, somewhat better, 2.2 percent. And even when preservatives were used, if we*

[82] Subcommittee on Human Rights and Wellness, Government Reform Committee, Mercury in Medicine Report, Washington, DC: Congressional Record, May 21, 2003:E1011-30.

look at the ampules, the number of lots that were rejected went from 5.6 to 4.4 with phenol, to 2.1 with organomercurial. In the multi-dose containers, it went from 2.2 down to 0.5 with phenol and 0.8 with the organomercurial... The reason I show these data is simply to point out that even with preservatives, there was still a number of lots that were rejected because of issues of stability. Now, today, these numbers are significantly lower, and if manufacturers would, you know, would do media fills to test the you know, the filling, and we're looking at numbers like one in ten.. However, I point this out simply to say that the numbers will not be zero and the risk of no preservative will be slightly greater than with the preservative.

Dr. Stanley Plotkin (Pasteur Merieux Connaught): *Pages 54-55: The published evidence that the Thimerosal contained in vaccines is dangerous is unconvincing...Yet, it [Thimerosal] remains the most active preservative and no equivalent substitute is available. Political concerns aside, it may be justified to keep [it] in some vaccine formulations, particularly those in multi-dose preparations. Beyond the factual scientific issues, the process of decision in this matter has been flawed. This meeting should have taken place before a public health decision or a public announcement was made. There should have been adequate consultation and discussion. This point of view probably gives offense to some, and I'm sorry that this should be the case as my remarks are not directed against any person in particular...However so far, manufacturers have seen no evidence for a clear and present danger, but, rather, a rush to judgment.*

Dr. C. John Clements: Pages 60, 68 (WHO): ***As you can see from this molecular description of Thimerosal, it's the mercury which is the pride and the downfall of this gentleman, and we can all agree, I think, right away, that the mercury here is not what we want in preservatives. There's ample evidence that it is an undesirable molecule which is taken in by the human through food and drink and pharmaceuticals and vaccines. In general terms, we're without hesitation in saying we don't want it, and that this is a strong basis for further action...*** *What immediate impact on developing countries would there be if Thimerosal were removed from vaccines? As Stan has already said, existing suppliers would be unable to supply such vaccines and supplies would rapidly dry up. Locally-produced vaccines, and remember I've identified them as being a major source in developing countries, would be unable to substitute for this preservative. Local production would either stop or - I'm not sure whether it's worse or about the same level of significance, but they might turn to producing without the preservative.*

Dr. Stanley Plotkin (Pasteur Merieux Connaught): Page 83: *In relation to Dixie Snider's comment, I would like to say that if anti-vaccinationists did not have mercury, they would have another issue, and one cannot prevent them from making hay regardless of whether the sun is shining or not. So I don't think that's really a valid reason for making decisions.*

Dr. Jeffery Englhardt (Eli Lilly): Pages 91-97: *When the question came to me about toxicity of Thimerosal, I had to scratch my head and wonder, what the heck is this? This is not a product that I have on my horizon very often, and I had to talk to one of my more senior colleagues who said, 'Oh, that's Merthiolate.' As I started getting into this particular topic, I had to go back into our corporate literature but also start searching*

*the scientific literature. Though we keep information from a material safety data sheet standpoint, we don't keep an active research program going on this compound, mostly because of its historical perspective....As Dr. Klein mentioned earlier, we were one of the first to be using Thimerosal as a preservative in some of our older vaccine days in terms of the diphtheria vaccine. It was also used in some of our other toxoids that were produced back in the '30s and '40s. And as mentioned also, this has been marketed since the '30s, and as I got into our literature, I found that there is very little in terms of toxicology in animals. Most of it is quite old – The primary reference is a 1931 reference in the American Journal of Hygiene - and it's often in obscure journals or cited as one or two sentences within review articles, and it's very difficult to find very explicit information on Thimerosal...**One thing that I did find is that the ethylmercury and thiosalicylate are the primary metabolites which were described in an article published from Lilly in 1956...It should also be noted that Thimerosal does cross the blood/brain barrier. It also crosses the placental barrier.***

In July 2000 the Government Reform Committee of the United States Congress held hearings on mercury. Congresswoman Helen Chenoweth-Hage (R-ID) stated [emphasis added]:

> *...I have a staffer who is in the Navy Reserve right now, but he used to be active with the airborne divisions, and he was in for a test in one of the medical military hospitals, and upon taking his temperature, they broke a thermometer, and mercury splattered across his glasses and some got in his eye. Well, the first thing they did was cutoff his clothes. The second thing was call in OSHA to clean up the mercury. And then they worked on him to make sure his eyes were irrigated, and you guys, you witnesses, absolutely amaze me. I wonder where the disconnect is, for Pete's sake. You listened to the testimony just as I did, and you are willing to, with a straight face, tell us that you are eventually going to phase this out after we know that a small baby's body is slammed with 62 times the amount of mercury that it is supposed to have, and OSHA reacts like they did in the case of this accident of this naval man. It doesn't make sense. No wonder people are losing fait in their government. And to have one of the witnesses tell us it is because mothers eat too much fish? Come on. We expect you to get real. We heard devastating testimony in this hearing today, and we heard it last April. And this is the kind of response we get from our government agencies? I am sorry. When I was a little girl, my daddy talked to me about something about a duck test. I would ask each one of you to read this very excellent work by Sallie Bernard and Albert Enayati, who testified here today. My daddy used to say if it walks like a duck and talks like a duck and sounds like a duck, for Pete's sake it is a duck. I recommend that you read this, side-by-side, page after page of analysis of the symptoms of people who are affected with mercury poisoning compared to autism. this is the duck test, and you folks are trying to tell us that you can't take this off the market when 8,000 children are going to be injected tomorrow; 80 children may be coming down, beginning tomorrow with autism? What if there was an E. coli scare? What if there was a problem with an automobile? There recall would be like that. We are asking you to do more than analyze it. We are asking you to*

> *tell this body and the American people that it is more than inconclusive. It passes the duck test, and we need you to respond. We need that to come off the market now because you think that we are elevating the case today? Just wait until it gets in the courts. This case could dwarf the tobacco case. And we would expect you to do something now before that circus starts taking place. Denial is not proper right now. You know, I still go back to the fact-I still want to talk about the duck test, Mr. Egan [FDA], I will address this to you. You know, it was shown in the last panel that autistic symptoms emerge after vaccination. It was shown that vaccines contain toxic doses of mercury. It was shown that autism and mercury poisoning, the physiological comparison is striking. There is altered neurotransmitter activity, abnormal brain neuronal organization, immune system disturbance, EEG abnormalities. It goes on and on and on, the comparisons. That is why I say, I back up what the Chairman and the ranking member are all asking you, that we cannot wait until 2001 to have this pulled off. You know, if a jury were to look at this, the circumstantial evidence would be overwhelming. Let's do something before we see it in the courts.*[83]

In 2001, van't Veen published regarding thimerosal [emphasis added]:

> *The very low thiomersal concentrations in pharmacological and biological products are relatively non-toxic, but probably not in utero and during the first 6 months of life. The developing brain of the fetus is most susceptible to thiomersal and, therefore, women of childbearing age, in particular, should not receive thiomersal-containing products.*[84]

How Did/Does Thimerosal Harm Children

In the early 1990s, at the same time that the rate of neurodevelomental disorders vastly increased in the United States, the amount of mercury from childhood vaccines approximately tripled with the addition of a full series of hepatitis B and Haemophilus Influenza Type b (Hib) vaccines to the required childhood vaccination schedule, so that children were exposed to **237.5 micrograms of ethylmercury** directly injected during the first 18 months of life (**187.5 micrograms of ethylmercury** in the first 6 months of life).[85]

Researchers have estimated hair mercury concentrations expected to result from the recommended CDC schedule during the 1990s utilizing a one compartment pharmacokinetic model, and found that modeled hair mercury concentrations in infants exposed to Thimerosal-containing vaccines were in excess of the Environmental Protection Agency (EPA) safety guidelines of 1 part-per-million (ppm) for up to 365

---

[83] Subcommittee on Human Rights and Wellness, Government Reform Committee. Mercury in Medicine Report. Washington, DC: Congressional Record, May 21, 2003:E1011-30.
[84] van't Veen AJ. Vaccines without thiomersal: why so necessary, why so long coming? Drugs 2001;61:565-72.
[85] Redwood L, Bernard S, Brown D. Predicted mercury concentrations in hair from infant immunizations: cause for concern. Neurotoxicology 2001;22:691-7.

days, with several peak concentrations within this period (some more than **10-fold** in excess of the EPA safety guidelines).[86] In examinations of first baby haircut mercury levels in a case-series of 45 non-autistic children, it has been shown that **more than 80%** of the young children clinically examined had hair mercury levels above the EPA safety guidelines, and some had hair mercury levels almost **20-fold** in excess of the EPA safety guidelines.[87] Other authors have examined the instantaneous relative excess doses of mercury children received from Thimerosal-containing childhood vaccines in comparison to Federal Safety Guidelines established for the oral ingestion of methylmercury, a similar compound to the ethylmercury in childhood vaccines.[88] The researchers reported that children as part of the CDC routine childhood immunization schedule from the 1990s received instantaneous doses of mercury from Thimerosal-containing childhood vaccines that were between **11- to 150-fold** in excess of the EPA oral ingestion of methylmercury safety guideline [0.1 µg mercury / Kg bodyweight / day] and **2.7- to 37-fold** in excess of the Food and Drug Administration (FDA) oral ingestion of methylmercury safety guideline [0.4 µg mercury / Kg bodyweight / day] at specific times during the first 5 years of life.

Researchers have reported that exposure to mercury can cause immune, sensory, neurological, motor, and behavioral dysfunctions similar to traits defining or associated with autistic disorders, and the similarities extend to neuroanatomy, neurotransmitters, and biochemistry.[89]

Population Epidemiological Studies Examining U.S. Children

In order to examine the relationship between Thimerosal-containing childhood vaccines and autistic disorders in the United States, a series of epidemiological studies based upon assessments of the Vaccine Adverse Event Reporting System (VAERS) database have been undertaken.[90] The VAERS database is an epidemiological database that was

[86] Redwood L, Bernard S, Brown D. Predicted mercury concentrations in hair from infant immunizations: cause for concern. Neurotoxicology 2001;22:691-7.
[87] Holmes AS, Blaxill MF, Haley BE. Reduced levels of mercury in first baby haircuts of autistic children. Int J Toxicol 2003;22:277-85.
[88] Geier MR, Geier DA. Thimerosal in childhood vaccines, neurodevelopment disorders, and heart disease in the United States. J Am Phys Surg 2003;8:6-11.
Geier DA, Geier MR. An assessment of the impact of Thimerosal on neurodevelopmental disorders. Pediatr Rehabil 2003;6:97-102.
[89] Bernard S, Enayati A, Redwood L, Roger H, Binstock T. Autism: a novel form of mercury poisoning. Med Hypotheses 2001;56:462-71.
Bernard S, Enayati A, Roger H, Binstock T, Redwood L. The role of mercury in the pathogenesis of autism. Mol Psychiatry 2002;7 Suppl 2:S42-3.
Blaxill MF, Redwood L, Bernard S. Thimerosal and autism? A plausible hypothesis that should not be dismissed. Med Hypotheses 2004;62:788-94.
[90] Geier MR, Geier DA. Thimerosal in childhood vaccines, neurodevelopment disorders, and heart disease in the United States. J Am Phys Surg 2003;8:6-11.
Geier DA, Geier MR. An assessment of the impact of Thimerosal on neurodevelopmental disorders. Pediatr Rehabil 2003;6:97-102.
Geier MR, Geier DA. Neurodevelopmental disorders after Thimerosal-containing vaccines: a brief communication. Exp Biol Med 2003;228:660-664.

established by an act of the United States Congress and specific vaccine-associated adverse events are required to be reported by law. The utility of VAERS in vaccine safety studies has been reviewed, and it has been used in previous vaccine epidemiological safety studies.[91] In studies examining the relationship between thimerosal and neurodevelopmental disorders based upon analysis of the VAERS database, the incidence rates of reported adverse events following Thimerosal-containing and Thimerosal-free DTaP vaccines administered for similar years and in similar childhood vaccination schedule have been compared. The results demonstrated that there were 2- to 8-fold statistically significantly increased risks for neurodevelopmental disorders, depending on the specific symptoms or disorder, reported to the VAERS database among children receiving Thimerosal-containing DTaP vaccines in comparison to children receiving Thimerosal-free DTaP vaccines, while other vaccine-associated adverse events not biologically plausibly linked to mercury, outcomes such as fever, injection site pain, and seizures, were reported similarly to the VAERS database following Thimerosal-containing and Thimerosal-free DTaP vaccines. In addition, ecological studies have assessed the population prevalence of autism and speech disorders in the United States in comparison to the average doses of mercury children received from Thimerosal-containing childhood vaccines.[92] It was observed that there was a statistically significant positive correlation between exposures to mercury from Thimerosal-containing childhood vaccines and the population prevalence of autism and speech disorders.

The only potential studies showing no relationship between Thimerosal and autism have been conducted in Denmark, Sweden and England.[93] These studies have very little

---

Geier DA, Geier MR. Neurodevelopmental disorders following Thimerosal-containing childhood immunizations: a follow-up analysis. Int J Toxicol (in press).

[91] Geier DA, Geier MR. A review of the Vaccine Adverse Event Reporting System database. Expert Opin Pharmacother 2004;5:693-8.

Chen RT, Rosenthal S. An errant critique that misses the mark. Arch Pediatr Adolesc Med 1996;150:464-5.

Lloyd JC, Haber P, Mootrey GT, Braun MM, Rhodes PH, Chen RT; VAERS Working Group. Adverse event reporting rates following tetanus-diphtheria and tetanus toxoid vaccinations: data from the Vaccine Adverse Event Reporting System (VAERS), 1991-1997. Vaccine 2003 Sep;21:3746-50.

Sever JL, Brenner AI, Gale AD, Lyle JM, Moulton LH, West DJ; Anthrax Vaccine Expert Committee. Safety of anthrax vaccine: a review by the Anthrax Vaccine Expert Committee (AVEC) of adverse events reported to the Vaccine Adverse Event Reporting System (VAERS). Pharmacoepidemiol Drug Saf 2002;11:189-202.

Rosenthal S, Chen R, Hadler S. The safety of acellular pertussis vaccine vs whole-cell pertussis vaccine. A postmarketing assessment. Arch Pediatr Adolesc Med 1996;150:457-60.

Haber P, Chen RT, Zanardi LR, Mootrey GT, English R, Braun MM; VAERS Working Group. An analysis of rotavirus vaccine reports to the vaccine adverse event reporting system: more than intussusception alone? Pediatrics 2004;113:e353-9.

[92] Geier MR, Geier DA. Thimerosal in childhood vaccines, neurodevelopment disorders, and heart disease in the United States. J Am Phys Surg 2003;8:6-11.

Geier DA, Geier MR. An assessment of the impact of Thimerosal on neurodevelopmental disorders. Pediatr Rehabil 2003;6:97-102.

Geier DA, Geier MR. A comparative evaluation of the effects of MMR immunization and mercury doses from Thimerosal-containing childhood vaccines on the population prevalence of autism. Med Sci Monit 2004;10(3):PI33-9.

[93] Andrews N, Miller E, Grant A, Stowe J, Osborne V, Taylor B. Thimerosal exposure in infants and developmental disorders: a retrospective cohort study in the United Kingdom does not support a causal association. Pediatrics 2004 Sep;114:584-91.

applicability to the US experience with Thimerosal, since in both Denmark, Sweden, and England much lower levels of Thimerosal were administered to children as part of the childhood immunization schedule. Overall, these countries administered approximately one-third the Thimerosal dose administered in the United States, and these countries administered the Thimerosal dose in a much less rigorous schedule than in the United States (i.e. in the US Thimerosal dosing began on the day of birth). Additionally, the studies in Denmark have been shown to suffer from the fact that (1) only inpatient diagnosed autistics were initially identified, and then latter in these studies both inpatient and outpatient diagnosed autistics were identified; (2) different diagnosis codes of neurodevelopmental maladies, i.e., psychosis infantilis posterior (ICD-8 299.01) versus atypical (i.e. regressive) autism (ICD-10 F84.1), before and during the presumed increase in autism incidence, respectively; and (3) data from additional clinics with a significant portion of the autistics in the entire country were added as the studies progressed.[94] Also, in considering the Stehr-Green et al. study, despite the fact that the authors presented data from Sweden and Denmark showing no relationship between Thimerosal and autism, they did present ecological epidemiological data from the United States, showing a direct relationship between the prevalence of autism and the amount of mercury children received from Thimerosal-containing vaccines.[95]

Clinical Epidemiological Studies of Mercury Body-Burden in Autistic Children

Researchers, including the *Chairman of the Department of Materials and Engineering at Arizona State University*, have evaluated the concentration of heavy metals in the urine among children with autistic spectrum disorders in comparison to a neurotypical control population.[96] Based on excretion following an identical three-day provocation with an oral chelation agent meso 2,3-dimercaptosuccinic acid (DMSA), it was observed that there was approximately 6-times statistically significantly greater urinary mercury concentrations among vaccinated autistic children matched to neurotypical vaccinated controls, whereas children with autistic spectrum disorders had similar urinary cadmium and lead concentrations in comparison to neurotypical controls. Similar urinary mercury concentrations were observed among matched neurotypical vaccinated and neurotypical unvaccinated children. This study concluded that the increased levels of urinary mercury

---

Heron J, Golding J; ALSPAC Study Team. Thimerosal exposure in infants and developmental disorders: a prospective cohort study in the United Kingdom does not support a causal association. Pediatrics 2004;114;577-83.

Hviid A, Stellfeld M, Wohlfahrt J, Melbye M. Association between Thimerosal-containing vaccine and autism. JAMA 2003;290:1763-6.

Madsen KM, Lauritsen MB, Pedersen CB, Thorsen P, Plesner AM, Andersen PH, Mortensen PB. Thimerosal and the occurrence of autism: negative ecological evidence from Danish population-based data. Pediatrics 2003;112:604-6.

Stehr-Green P, Tull P, Stellfeld M, Mortenson PB, Simpson D. Autism and Thimerosal-containing vaccines: lack of consistent evidence for an association. Am J Prev Med 2003;25:101-6.

[94] Geier DA, Geier MR. Neurodevelopmental disorders following Thimerosal-containing childhood immunizations: a follow-up analysis. Int J Toxicol (in press).

[95] Stehr-Green P, Tull P, Stellfeld M, Mortenson PB, Simpson D. Autism and Thimerosal-containing vaccines: lack of consistent evidence for an association. Am J Prev Med 2003;25:101-6.

[96] Bradstreet J, Geier DA, Kartzinel JJ, Adams JB, Geier MR. A case-control study of mercury burden in children with autistic spectrum disorders. J Am Physicians Surg 2003;8:76-9.